

# **Progress Towards Elimination of Perinatal HIV Infection in the United States**

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Today I will present population-based HIV/AIDS surveillance data highlighting and updating the remarkable changes in the epidemiology of perinatal HIV infection and recent efforts to significantly reduce perinatal HIV transmission. These data suggest it may be possible to consider the goal of elimination of perinatal HIV infection in the U.S. But, challenges still remain.

The public health definition of elimination is the reduction to zero of the incidence of infection caused by a specific agent in a defined geographic area as the result of deliberate efforts; continued measures to prevent reestablishment of transmission are required.

An elimination program requires a highly efficacious intervention. In 1994, maternal and neonatal zidovudine use in PACTG 076 reduced mother-to-child transmission by 67%. Since then, clinical trials in international settings have shown that abbreviated antiretroviral regimens, such as short course zidovudine and intrapartum regimens such as Nevirapine, are also effective in reducing perinatal transmission. Combination antiretroviral therapy for the mother's health that reduces viral load to undetectable levels may lower the risk of transmission to < 1% and elective cesarean section combined with ZDV reduced rates to 1-2%. Thus, multiple effective strategies are now available to reduce mother-to-child HIV transmission.

Surveillance is a critical part of an elimination program and must be used to guide program strategy. The efforts in each of the states to use the enhanced HIV surveillance data for targeting and evaluating local programmatic efforts are essential. Enhanced surveillance efforts are needed with successive stages of elimination. Highly effective implementation efforts are also essential.

The U.S. Public Health Service issued recommendations in 1994 for ZDV use and in 1995 for universal prenatal HIV counseling and voluntary testing. In 1998, the Institute of Medicine reported widespread implementation of these recommendations, but barriers, such as the lack of routine, voluntary prenatal HIV testing and of prenatal care, remain. To address these barriers and further reduce perinatal transmission, CDC funded both programmatic and surveillance efforts in states with the highest burden of disease.

## **Progress Towards Elimination**

Three sources of state-level data allow us to assess progress towards elimination. Enhanced perinatal HIV surveillance was previously conducted in seven states with HIV reporting. In addition to active HIV case surveillance, these states matched HIV/AIDS and birth registries for infant birth years 1993 and 1995-1997 to identify additional mother-infant pairs. Maternal HIV clinic, prenatal, labor and delivery, and newborn and pediatric records were reviewed to provide more complete and accurate data. Now, enhanced perinatal surveillance has been expanded to 22 states.

Data were also evaluated from 33 states that conduct routine, active HIV case surveillance and monitor

prenatally- exposed children for their HIV status. Data are collected on demographics, prenatal care, illicit drug use during pregnancy, maternal HIV testing, antiretroviral use, birth history, and HIV status.

Finally, we evaluated national AIDS surveillance data on prenatally-acquired AIDS cases reported through December 2000 to look at trends in diagnoses through June 2000, adjusting for reporting delay and risk redistribution. To estimate perinatal HIV incidence in the U.S., the birth distribution of prenatally- acquired AIDS was adjusted for time to AIDS and reporting delay.

Of course the most important perinatal prevention strategy is to prevent HIV infection in women. Through June 2000, 753,907 cases of AIDS have been reported, and 438,795 deaths. In association with the widespread use of highly active antiretroviral therapy, a marked decline in AIDS incidence and deaths began in 1996 and continued into 1998. However, rates of decline in AIDS incidence and deaths slowed during the latter part of 1998 and 1999, probably for several reasons (limits of treatment in extending survival, failing therapies due to resistance, late HIV testing, inadequate adherence or access to therapies, and a recent increase in incidence in some risk groups). AIDS prevalence continues to rise, with approximately 320,000 persons living with AIDS at the end of 1999.

Women account for 17% of all AIDS cases and 20% of all prevalent cases. Over 64,000 women were living with AIDS in 1999. Most women with AIDS are members of racial or ethnic minorities. During the 1990's, women, minorities and persons infected through heterosexual contact represented a growing proportion of annual AIDS cases.

Over 16,000 women 15-34 years of age were reported to be living with AIDS in the United States at the end of 1999. These women are of childbearing age and in the years of highest fertility. States with HIV case surveillance data are better able to target programs and services to these women to enhance efforts to further reduce transmission to their newborns.

The 32 areas that conduct name-based confidential HIV infection surveillance of adults and adolescents reported an additional 15,190 women in this age group living with HIV infection. In most states with HIV surveillance, the number of infected women who have not developed AIDS exceeds the number of women with AIDS. These numbers indicate the current burden of HIV morbidity and the substantial need for medical and social services for these women, currently and in the future.

The number of young women living with HIV in the South is quite striking. A large number of HIV-infected women reside in states that do not have HIV surveillance, and undoubtedly there are many infected women who have not been tested. Thus, the HIV numbers are underestimates of the true HIV-infected population.

Perinatal AIDS cases rose rapidly through the 1980's, peaked in 1992 (N=909), and then declined 81% following PACTG 076 and the PHS recommendations to a low in 1999 (N=171). Declines occurred in all racial and ethnic groups, where the majority of cases occur in African American and Hispanic children, and in all age groups. Some of the most recent declines may also be due to improved therapy of HIV-infected children. Reflecting recent perinatal prevention efforts, the largest declines occurred earliest among infants and also those diagnosed at 1-5 years who were born in more recent years.

Trends declined in all regions. CDC estimates that there were 1,200 HIV-infected children born in 1992, which decreased to an estimated 400 and less born in recent years. Of prenatally- acquired AIDS cases born in 1997-1998 and reported to CDC, one-third involved mothers who were tested for HIV after the

child's birth; only 13% of these women received ZDV in pregnancy, 23% of the infants received ZDV neonatally, and 60% of the infants were not tested for HIV in the first 2 months of life. Thus, although the successes are dramatic there are still missed opportunities for prevention.

### **Can More Cases Be Prevented?**

Perinatal transmission of HIV can be prevented by interventions during the prenatal, perinatal, or postnatal periods. However, these interventions cannot be successful unless the HIV-infected woman is in prenatal care, is offered and accepts an HIV test, is offered and accepts ZDV, and adheres to the drug regimen. In addition, providers and clients are responsible for adherence to regimens during the intrapartum and neonatal periods, and the mother and infant must receive follow-up care. Mothers must also avoid breast-feeding.

It is important to evaluate all available surveillance data at the local, state or national level to characterize the perinatal HIV epidemic and to target and evaluate prevention efforts. This includes data on:

- prenatal care:
  - general population: birth certificates, Pregnancy Risk Assessment Monitoring System (PRAMS)
  - HIV-positive women: enhanced perinatal HIV surveillance
- HIV counseling and testing:
  - all pregnant women: birth certificates, PRAMS, audit of hospital birth records–Emerging Infectious Disease Program (EID) sites
  - HIV-positive women: enhanced perinatal HIV surveillance
- use of antiretroviral therapy:
  - enhanced perinatal HIV surveillance, Serosurvey of Childbearing Women (SCBW)
- outcome of child
  - enhanced perinatal HIV surveillance
- other sources: Medicaid data, Supplement to HIV/ AIDS Surveillance (SHAS), HIV counseling and testing data, Adult Spectrum of Disease (ASD), Pediatric Spectrum of Disease (PSD).

Analysis of data from the Behavioral Risk Factor Surveillance System (BRFSS), a telephone interview survey of a random sample of adults aged 18 years and older, showed that the proportion of pregnant women tested for HIV increased from 1994 to 1996 (42.6% to 53.1%), and then again from 1997 to 1998 (51.7% to 55.9%). The proportion of pregnant women who reported pregnancy as the reason for their test increased from 60% in 1994 to 84% in 1999. Pregnant women were more likely to be tested if they lived in the South, were not working, were 18- to 24-years-old, never married or had health insurance.

Preliminary data from a birth audit conducted on a random sample of maternal delivery records for 1998 and 1999 births from three states (Georgia, Minnesota, and Connecticut) in the Emerging Infectious Program Network indicate that, in contrast to extremely high testing rates documented for syphilis, testing for HIV was much less complete and varied by state, from less than 40% in Connecticut to over 60% in Georgia.

The pregnancy risk assessment monitoring system (PRAMS) is an ongoing population-based surveillance system of women who recently delivered a live-born infant. The sample is drawn from birth

certificates 2-4 months after birth; women are mailed a questionnaire and followed up by telephone. Responses from mothers who sought prenatal care during their pregnancy indicated that offers of testing and counseling for HIV varied by state (60%-80%), but that a substantial proportion of mothers did receive prenatal HIV test counseling and a high proportion of mothers accepted the test (1998 estimates available for 11 states).

For the perinatal HIV guidelines evaluation project, 1,362 women in four states were interviewed 24-48 hours postpartum. Although 82%-92% were offered an HIV test, the proportion tested differed dramatically by site (46%-86%; 75% overall). There was a higher proportion tested among those offered the test as well as among those whose provider recommended the test.

Pregnancy rates in HIV-infected women enrolled in the adult and adolescent spectrum of disease project (ASD) did not change significantly during 1996-1998 compared with 1991 through 1995. However, pregnancy rates did increase significantly from 1996 to 1998. Women who received HAART were more likely to become pregnant compared to women who were receiving other antiretroviral therapies. Pregnancy rates were highest among women 15-24, and were higher for black women than white women.

Data on 1,431 HIV-infected mothers who gave birth in 1995-1997 in the seven states that conducted enhanced perinatal surveillance indicate that 13% had no prenatal care and an additional 9% had only 1-2 visits; 2% of women in the general population had none or only 1-2 visits. Women who use illicit drugs in pregnancy are at high risk for not receiving prenatal care. In these seven states in 1995-1997, 83% of HIV-infected mothers with no prenatal care used illicit drugs in pregnancy, compared with 23% of those with 3 or more prenatal care visits. Mothers with less prenatal care were also less likely to have received prenatal ZDV, but rates differed markedly among states.

Once in prenatal care, women need to be offered and need to accept HIV testing. States with enhanced perinatal HIV surveillance have data on 88% of HIV-positive women delivering in those states. Thus, we analyzed trends in maternal HIV testing of the reported mothers in these states. The proportion diagnosed with HIV before giving birth increased from 84% in 1993 to 89% in 1996 and remained stable in 1997. The percentage of those tested after birth declined, but 4%-5% of women continued to be tested at delivery, and 6% of the mothers were tested after birth in 1996 and 1997. Data from states with HIV surveillance also indicate an upward trend between 1994 (76%) and 1999 (92%) in percentage of women diagnosed prior to giving birth.

Of 8,306 HIV-exposed deliveries in 33 states with HIV surveillance, the percentage of deliveries by cesarean section increased from around 15% in the first half of 1994 to nearly 50% in the first half of 2000. Data reported for over 8,500 prenatally-exposed children born to HIV-positive mothers diagnosed with HIV before or at birth demonstrate rapid uptake of recommended ZDV therapy from 1994-1996 with a relative leveling since 1997. Receipt of any component of the recommended ZDV regimen increased from 37% of children born in 1994 to 90% in 1997 and then leveled; receipt of prenatal ZDV increased from 30% in 1994 to 71% in 1996 and then leveled. Increasing numbers of HIV-infected women are receiving combination therapy during pregnancy for their own health: 39% in 1998 and 52% in 1999 and almost 60% in the first half of 2000. Between 1994 and June 2000, only 0.9% of women refused ZDV in pregnancy; of these, 77% accepted ZDV treatment for their newborns. In recent years, only 15%-17% of HIV-infected pregnant women had no antiretroviral therapy.

The increasing proportion of HIV-infected mothers and their infants who have received any ZDV

has resulted in declining perinatal HIV transmission and a dramatic decline in AIDS cases among these infants. Data from the 33 states reporting HIV infection demonstrate declines in perinatal HIV infection rates. Of children first evaluated for HIV at less than two months of age, 22% were infected in 1993; this percentage declined to 9.5% in 1996, then 7% in 1998, to an all-time low of 4.4% in 1999. Follow-up still continues. Based on data from states with enhanced perinatal surveillance, receiving all three components of ZDV was associated with a 68% reduction in transmission of HIV to the infant.

Despite dramatic declines, cases of perinatal HIV infection continue to occur, mostly because of missed opportunities for prevention. We examined 227 HIV-infected children born from 1995 to 1997 in the states with enhanced surveillance. Our findings:

- prenatal care
  - 14% had none; 26% unknown
  - of those who received care, 14% had <2 visits
- maternal HIV testing
  - 20% tested after delivery
  - 7% tested at delivery
- antiretroviral therapy
  - of mothers tested before delivery and who had received prenatal care, 22% were not prescribed prenatal ZDV
- 29% had all 3 prevention interventions: prenatal care, HIV test before birth, prescribed prenatal, intrapartum and newborn ZDV.

### **Current Trends and Concerns**

Prenatally-acquired cases of AIDS have declined dramatically since peaks in 1992-1994. Among children 1-4 years of age, annual rates of death per 100,000 population from AIDS increased from 1987 to 1995 and then declined dramatically through 1998. Based on increasing survival, we estimate that approximately 10,000 children are living with perinatal HIV infection, of whom approximately 2,200 are adolescents. Targeted education and prevention strategies surrounding sexual health, prevention of ongoing sexual transmission and improved adherence with complex treatment regimens are critical.

An ongoing concern is the potential toxicity of drugs administered in the perinatal period. Nucleoside reverse transcriptase inhibitors (NRTI) have known toxicity to the mitochondria: ZDV and other NRTI's inhibit mitochondrial DNA polymerase gamma. In February 1999, two HIV-uninfected infants prenatally-exposed to ZDV + 3TC were reported to have died of progressive neurologic disease associated with mitochondrial dysfunction (*Lancet* 1999;354:1084-9). They were both one-year old.

A perinatal safety review working group examined all deaths among HIV-exposed children who died at less than 5 years of age in five U.S. cohorts, including those reported through pediatric HIV surveillance. Among over 20,000 children born to HIV-infected women, over half of whom had been exposed to NRTI's, 223 died. None died of mitochondrial dysfunction consistent with those cases presented by the French investigators. However, innovative surveillance strategies are needed to follow potential adverse events from perinatal antiretroviral drug exposure.

### **Conclusion**

The data I have presented show rapid implementation of Public Health Service guidelines and a recent

leveling in rates of receipt of antiretroviral therapy and of prenatal HIV testing. Substantial declines in prenatally- acquired AIDS and perinatal HIV infection rates were coincident with increasing ZDV use. Missed opportunities occurred among high risk women: those without prenatal care, particularly illicit drug users, and those who present in labor with unknown HIV status.

In order to eliminate perinatal HIV transmission, in addition to continued sustained efforts, intensive new programmatic efforts are needed to reach these high-risk HIV-infected women, including public information campaigns and outreach to increase access to prenatal care. Future efforts should include education and training of providers to offer prenatal HIV counseling and voluntary testing as a standard of care and operational research to implement rapid HIV testing and institution of ART during the intrapartum period for women without prenatal care. Enhanced perinatal HIV surveillance, expanded to 22 states, will help target these efforts and will help evaluate the extent that intensified prevention programs contribute to reduced transmission. Innovative surveillance strategies are needed to monitor antiviral resistance and potential toxicities. Clearly, prevention of HIV infection in women is critical. Most importantly, a global effort to address the ever growing perinatal HIV epidemic in the rest of the world is urgently needed, both to extend benefits seen in U.S., and to develop effective strategies for resource-poor countries.